Amendments to the Specification:

Please replace the paragraph beginning at line 16 with the following:

One potentially successful repair solution seeks to mimic the success of autografts by removing cells from the patient by biopsy and growing sufficient quantities of mineralized tissue *in vitro* on implantable, three-dimensional scaffolds for use as a functionally equivalent autogenous bone tissue. In this way, an ideal bony repair environment is created by reproducing the intrinsic properties of autogenous bone material, which include: a porous, three-dimensional architecture allowing osteoblast, osteoprogenitor cell migration and graft re-vascularization; the ability to be incorporated into the surrounding host bone and to continue the normal bone remodeling processes; and the delivery of bone forming cells and osteogenic growth factors to accelerate healing and differentiation of local osteoprogenitor cells (Burwell, R.G.. History of bone grafting and bone substitutes with special reference to osteogenic induction, in ~~Bon~~ Bone Grafts, Derivatives and Substitutes., M.R. Urist and R.G. Burwell, Editors. 1994, Butterworth-Heinemann Ltd.: Oxford. p.3; Gadzag et al. J. Amer. Acad. Ortho. Surg. 1995 3(1):1).

Please replace the paragraph beginning at line 2 of page 3 with the following:

Biodegradable scaffolds for *in vitro* bone engineering, which possess a suitable three-dimensional environment for the cell function together with the capacity for gradual resorption and replacement by host bone tissue have also

been described. See, e.g. ~~Cassebette~~ Casser-bette et al. Calcified Tissue International 1990 46(1):46-56; Masi et al. Calcified Tissue International 1992 51(3):202-212; Rattner et al. In Vitro Cellular & Developmental Biology-Animal 1997 33(10):757-762; Mizuno et al. ~~Bon~~ Bone 1997 20(2):101-107; ~~Elghannam~~ El-Ghannam et al. J. Biomed. Mater. Res. 1995 29(3):359-370; Ducheyne et al. J. Cell. Biochem. 1994 56(2):162-167; ~~Ishuag~~ Ishaug et al. J. Biomed. Mater. Res. 1997 36(1):17-28; ~~Ishuag~~ Ishaug -Riley et al. Biomaterials 1998 19(15):1405-1412; Goldstein et al. Tissue Engineering 1999 5(5):421-433; Devin et al. J. Biomater. Science-Polymer Edition 1996 7(8):661-669; Laurencin et al. Bone 1996 19(1):S93-S99; Thomson et al. Biomaterials 1998 19(21):1935-1943; and Laurencin et al. J. Biomed. Mater. Res. 1996 30(2):133-138. This three-dimensional matrix milieu provides the necessary microenvironment for cell-cell and cell-matrix interaction, and is sufficient for the production of limited amounts of mineralized bone matrix in static culture. To demonstrate clinical feasibility of tissue engineered bone and to sufficiently match the intrinsic properties of autogenous bone graft material, however, rapid mineralization of osteoid tissue grown *in vitro* must be achieved. In the above-described three-dimensional matrices, nonhomogeneous cell seeding confines cell density to the near surface of the scaffold and mineralized tissue formation is limited by inadequate diffusion of oxygen, nutrients, and waste.

Please replace the paragraph beginning at line 6 of page 4 with the following:

Formation of three-dimensional assemblies for culturing of various cell types in a rotating bioreactor have been described. See e.g. Goldstein et al. Tissue Engineering 1999 5(5):421-433; Granet et al. ~~Medical & Biological Engineering and Computing~~ Cell Eng. 1998 36(4):513-519; Klement et al. J. Cellular Biochem. 1993 51(3):252-256; Qui et al. Tissue Engineering 1998 4(1):19-34; Lewis et al. J. Cellular Biochem. 1993 51(3):265-273; Becker et al. J. Cellular Biochem. 1993 51(3):283-289; and Prewett et al. J. Tissue Culture Methods 1993 15:29-36. Using such assemblies, it has been shown that osteoblast-like MC3T3 cells form cell aggregates when grown on non-degradable microspheres and produce collagen fibrils in the matrix between microspheres (Klement et al. J. Cellular Biochem. 1993 51(3):252-256). Also, rat stromal cells cultured for 2 weeks on cytodex-3 beads formed aggregates, began synthesizing mineralized matrix and showed elevated expression of type I collagen and osteopontin (Qui et al. Tissue Engineering 1998 4(1):19-34). However, when microspheres with greater density than the surrounding medium are placed in a rotating bioreactor, centrifugal force induces heavier-than-water microspheres to move outward and collide with the bioreactor wall. These collisions induce cell damage and are a confounding variable in tissue engineering.

Please replace the paragraph beginning at line 4 of page 7 with the following:

It has been shown previously that when osteoblast cells are co-inoculated with microcarriers in a rotating bioreactor a random aggregation occurs generated by the adherence of cells to microcarrier beads and the formation of cellular bridges between adjacent microcarriers (Granet et al. ~~Medical & Biological Engineering & Computing~~ Cell Eng. 1998 36(4):513-519; Qiu et al. Tissue Engineering 1998 4(1):19-34; and Watts et al. Critical Reviews in Therapeutic Drug Carrier Systems 1990 7(3):235-259). However, this random aggregation that occurs in the rotating bioreactor is not conducive to strict quantitative comparison, because the size and shape of cell-bead aggregates as well as the degree of aggregation varies greatly. Such a limitation is overcome by the present invention via the sintered pre-assembly of microcarriers into dimensionally reproducible cell scaffolds prior to culture in the bioreactor. Furthermore, the microcarrier sintering method of the present invention is not limited by the adverse effects associated with the particulate leaching and consequently no unwanted degradation of the scaffold occurs during fabrication.

Please replace the paragraph beginning at line 18 of page 19 with the following:

Alkaline Phosphatase (ALP) activity was measured by using adaptations of standard histochemical (~~Vaan~~ Van Belle, H. Biochimica et Biophysica Acta 1972 289:158-168) and colorimetric (Rattner et al. In Vitro Cellular & Developmental Biology - Animal 1997 33(10):757-762) methods. At days 3 and 7, scaffolds were removed from both

the rotating and non-rotating bioreactor vessels and washed two times with PBS. Scaffolds were then incubated for 30 minutes at 37°C with Napthol AS-BI (Sigma, N-2250) phosphate salt (0.5 mg/ml; Sigma) and N,N-Dimethyl Formamide (10 µg/ml; Sigma D-8654) in 50 mM Tris buffer (pH 9.0), in the presence of Fast Red (Sigma, F-2768) violet salt (1.0 mg/ml). After 30 minutes, cells were washed two times with PBS and fixed by incubation in 2% paraformaldehyde for 30 minutes at 4°C. ALP staining was viewed by light microscopy. Scaffolds were fractured into halves in order to visualize cells in the interior regions of the 3-dimensional structure.